REMARKS

Claims 56-66, 68-77, 79-84, and 86-89 are currently pending in this application upon entry of this paper. Applicants have canceled claims 1-55, 67, 78, 85, and 90-119 without prejudice. Applicants reserve the right to file one or more continuation, divisional, or continuation-in-part applications to any canceled or withdrawn subject matter. No new matter has been added by the amendments.

I. The Rejections Under 35 U.S.C. § 112

A. The Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 56-61, 64, 65, 67,69-73, 76, 78, 80-83, 85 and 87-89 are rejected on pages 2-3 of the office action under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Without acquiescing to the propriety of the rejection, Applicants respectfully submit that they have amended independent claims 56, 57, and 58 thereby overcoming the rejection to these claims as well as claims dependent therefrom. Applicants respectfully request that the rejection of claims 56-61, 64, 65, 67,69-73, 76, 78, 80-83, 85 and 87-89 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement be reconsidered and withdrawn.

Claims 56-61, 64, 65, 67,69-73, 76, 78, 80-83, 85 and 87-89 are rejected on pages 3-4 of the office action under 35 U.S.C. § 112, first paragraph, as failing to reasonably provide enablement for all lipophilic groups.

Without acquiescing to the propriety of the rejection, Applicants respectfully submit that they have amended independent claims 56, 57, and 58 thereby overcoming the rejection to these claims and claims dependent therefrom. Applicants respectfully request that the rejection of claims 56-61, 64, 65, 67,69-73, 76, 78, 80-83, 85 and 87-89 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement be reconsidered and withdrawn.

B. The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 67, 78, and 85 are rejected on page 4 of the office action under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the office action alleges that the claims recite, "the covalent bond is in a position to improve activity and transport of the drug into a cell," and it is unclear what is intended by the phrase because the present specification lacks definition/identification of said position(s).

Without acquiescing to the propriety of the rejection, Applicants respectfully submit that they have canceled claims 67, 78, and 85 thereby rendering the rejection to these claims moot.

II. The Rejection Under 35 U.S.C. § 102(b)

Claims 57-61, 64, 65, 67, 72, 73 and 76 are rejected on page 5 of the office action under 35 U.S.C. 102(b) as allegedly being anticipated by Aszalos *et al.* (Biochemical Pharmacology, 1995) ("Aszalos"). In particular, the office action alleges that Aszalos teaches the antitumor activity of N-acylated daunorubicins and that longer fatty acid derivatives, such as N-octanoyl and N-dodecanoyl daunorubicins, were not substrates for P-glycoprotein, a cause of resistance to chemotherapeutic agents (see page 889, col. 1, 1st paragraph). Therefore, the office action alleges that the method of use taught by the reference is encompassed by the instant claims.

Applicants respectfully submit that the claims as amended are not disclosed or suggested by the instant claims. In particular, Aszalos fails to disclose a method wherein an active agent has a covalent bond to a lipophilic moiety, wherein said lipophilic moiety is a cis- or trans-n-9 monounsaturated fatty acid, fatty acid alcohol or fatty amine having a chain length of 18 or 20 carbon atoms.

Applicants respectfully request that the rejection of claims 57-61, 64, 65, 67, 72, 73 and 76 under 35 U.S.C. 102(b) as allegedly being anticipated by Aszalos be reconsidered and withdrawn.

III. The Rejection Under 35 U.S.C. § 103(a)

Claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85, and 87-89 are rejected on pages 5-6 of the office action under 35 U.S.C. § 103(a) as allegedly obvious over Aszalos. The office action alleges that the instant claims differ from the reference by reciting additional lipophilic derivatives of daunorubicin, for example, the C-18 unsaturated fatty acid derivates, and Aszalos teaches longer fatty acid overcome the resistance caused by over expression of P-glycoprotein ("PGP") in cancer cells. Therefore, according to the office action, the skilled artisan in the art would have been motivated to produce other N-acylated derivatives of daunorubicins utilizing other longer fatty acids with the reasonable expectation that the compounds produced would not be substrates for P-glycoprotein and, thus, be useful in treating patients with resistance to daunorubicin.

Applicants respectfully submit that Aszalos discloses the investigation of the behavior of N-octanoyl-daunorubicin ("N-C8-D") and N-dodecanoyl-daunorubicin ("N-C12-D") along with that of N-acetyl-D with respect to PGP, a product of multi drug resistance ("MDR") gene-expressing cells. (*Id.*). According to Aszalos PGP decreases intracellular concentration of these agents, possibly by facilitating active efflux; however, the mechanism by which this active efflux occurs is not well known. (*Id.*). Aszalos further discloses " [r]esults showed that N-acetyl-daunorubicin is a substrate, but the longer fatty acid derivatives, N-octanoyl- and N-dodecanoyl-daunorubicin, are not." (*Id.* at Abstract). Aszalos then concludes that the longer fatty acid derivatives interact with plasma membranes in a way that affected PGP function.

Applicants point out the term "longer fatty acid derivatives" in Aszalos is a relative term comparing N-acetyl-D to N-C8-D and N-C12-D, respectively. This is not a general suggestion that all longer chain fatty acids are applicable. Moreover, the use of longer fatty acid derivatives, particularly, N-C8-D and N-C12-D, is disclosed to reduce the instances of multidrug resistance not treat cancer generally. In fact, Aszalos shows that using longer chain fatty acids may not even be as good as shorter chain. Particularly, Figure 2 illustrates the effects of drug alone (solid bar) and drug plus cyclosporin A (open bar); C12-D alone and C12-D with cyclosporin basically

had the same effect, whereas D alone show improvement when combined with cyclosporin A and C2-D also showed reduction in cell count upon addition of cyclosporin. (*See* Aszalos at page 890).

Applicants respectfully submit that the assertion that Aszalos suggests covalently bonding a cis- or trans-n-9 chain of 18 or 20 carbon atoms to an active agent is not legally supported by the disclosure of Aszalos. Indeed, the Federal Circuit recently stated that the test for *prima facie* obviousness in an invention concerning chemical compounds "is consistent with the legal principles enunciated in *KSR*," and thus, "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a *prima facie* obviousness of a new claimed compound." *See Takeda Chemical Industries, LTD et al. v. Alphapharm PTY., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007) *citing KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1739 (2007).

Nothing in Aszalos discloses or suggests modifying the disclosure of Aszalos to contrive an active ingredient covalently bonded a cis- or trans-n-9 monounsaturated fatty acid, fatty acid alcohol or fatty amine having a chain length of 18 or 20 carbon atoms. To jump to the conclusion that the comparative data in Aszalos would suggest the claimed invention is not legally justified. Nothing in Aszalos would suggest using a longer chain length lipophilic agent than C-12, much less a cis- or trans-n-9 chain of 18 or 20 carbon atoms.

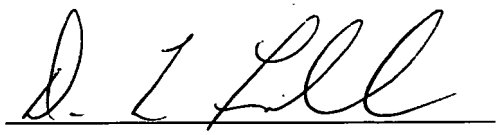
Applicants respectfully submit that for at least the above reasons, claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85, and 87-89 are not obvious under 35 U.S.C. § 103(a) over Aszalos. Applicants respectfully request that the rejection be reconsidered and withdrawn.

IV. Conclusions

Should the Examiner disagree with any of the above arguments, Applicants respectfully request a telephone interview with the Examiner and undersigned attorney for Applicants to advance the prosecution of the application.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a Constructive Petition for Extension of Time in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,



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